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Estimation of a minimum laser power with wavelengths of 1.47, 1.56, and 1.68 μm for efficient obliteration of varicose veins

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Abstract. **Experiments modelling endovenous laser obliteration (EVLO) are performed. As a result, laser radiation powers P_c at which collagen denaturation, tissue necrosis, and *vasa vasorum* destruction occur throughout the entire venous-wall thickness and, at the same time, the surrounding tissues are not subjected to unnecessary heating, are found. The main criterion for determining P_c is the achievement of 100% denaturation of venous-wall proteins, confirmed by morphological and calorimetric analysis. The P_c values for laser wavelengths of 1.47, 1.56, and 1.68 μm are found to be 6.0 ± 0.2, 5.0 ± 0.2, and 6.0 ± 0.2 W, respectively. It is established for all wavelengths in use that the temperature of the external venous-wall surface reaches 91 ± 2 °C at the corresponding power P_c. We relate the dependence of P_c on the radiation wavelength to the formation of a coagulum on the optical fibre tip moving through a blood-filled vessel. The achievement of temperature necessary for coagulum formation is determined by the simultaneously occurring processes of energy absorption and its dissipation in the form of heat. These processes become more intense with an increase in the absorption coefficient of the medium. A mechanism is proposed to explain the relationship between the P_c value and laser wavelength, based on the influence of the absorption coefficient of medium (blood) on the temperature near the fibre tip.**

Keywords: *laser heating, energy absorption and dissipation, venous wall, collagen denaturation, obliteration of varicose veins.*

1. Introduction

When using laser irradiation in medicine, the optimal radiation parameters (wavelength, exposure time, power, irradiation geometry, etc.) are chosen in correspondence with the stated purpose [1]. Laser technologies cannot be advanced successfully into in medical practice without simulating the physicochemical processes occurring in irradiated biological systems. The following steps are important for *ex vivo* studies. First, the critical changes in tissue, which would provide the target effect *in vivo* with minimally possible changes in the surrounding tissues, must be found. Second, it is necessary to establish the causal relationship between the experimental criterion and impact characteristics.

Endovenous laser obliteration (EVLO) belongs to methods of minimally invasive therapy of varicose veins; its essence is a thermal impact on vessel walls from inside with the aid of an optical fibre moving along a vein [2–5]. Cell destruction and thermal degradation of venous wall is the primary target effect of the procedure, which provides subsequent occlusion and obliteration of incompetent venous vessel [4, 5]. In this case, excessive heating increases the risk of undesirable complications, such as venous wall perforation and extensive inflammatory process, related to overheating of the paravenous region [6]. Obviously, the conversion of laser energy into heat and delivery of the obtained thermal energy to venous wall determine the achievement of the direct result of laser impact and the target effect of the procedure.

To optimise the laser impact on tissue, the laser wavelength and power are varied, both in experimental studies and in model calculations [5–12]. Lasers with wavelengths ranging from 1.32 to 1.9 μm turned out to be more efficient than those with wavelengths in the range of 0.81–1.06 μm [4, 5, 7, 9], because they provide the desired effect at a lower power. Due to this, the number of tissue perforations and other undesirable effects caused by tissue overheating decreases essentially. However, no significant differences in the action of radiation with different wavelengths on tissue were revealed. Model simulations showed the formation of a blood coagulum on the fibre tip. This coagulum becomes carbonised [11] and absorbs a significant part of radiation, as a result of which the temperature on the vein wall surface is independent of wavelength at the same radiation power [11, 12]. Nevertheless, studies aimed at searching for sources with the most appropriate radiation wavelength are continued. For example, it was proposed to use laser radiation with a wavelength of 1.9 μm in the latest publications [9, 10]; in authors' opinion, its higher efficiency is related to the larger value of water absorption coefficient. In any case, the issue of choice of the optimal radiation wavelength used in the EVLO procedure remains unresolved, and it can be solved based on more detailed understanding of the tissue heating mechanism.

The main purpose of our study was to determine the minimum laser power necessary for achieving the primary target effect of endovenous laser treatment of vein. This analysis is performed for laser radiations with wavelengths of 1.47, 1.56,

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and 1.68 μm. The changes in the wall vessel, accompanying this process, are estimated. To monitor these changes, we used thermal analysis, which allows one to determine the content of collagen as the main component of venous wall in the native form, and compared the result with the data on the state of collagen, cells, and *vasa vasorum* in tissue, obtained by histological analysis as a golden standard.

2. Experimental

The objects of study were 110 fragments of varicose veins of great saphenous veins, removed during phlebectomy.

A schematic of the experimental setup is presented in Fig. 1. To simulate EVLO *ex vivo*, a 5-cm-long vein segment (*1*) was extracted from a fragment and fixed in a plastic cylindrical container (*2*) on 1.5-cm-long tubes inserted in the container base. The container had a 1-mm-wide upper slit (*3*) oriented along the cylinder generatrix; the vein was installed so as to make its upper surface contact partially the slit. The container was filled with a 0.9% aqueous solution of sodium chloride, and the slit was covered by a 100-μm-thick propylene film (*4*) to exclude water evaporation from the venous wall surface during its heating. The venous vessel was filled with heparinised blood, and a quartz optical fibre (*5*) with a diameter of 600 μm (numerical aperture 0.22) and a bare tip (for laser radiation input) was inserted into it. Switching on the laser and automatic fibre pulling back (with a velocity of 0.7 mm s^{-1}) along the venous vessel occurred simultaneously.

The adequacy of the experimental model to the EVLO conditions *in vivo* was discussed in [13].

Three laser radiation sources with different wavelengths were used in the experiments: a diode laser with $\lambda = 1.47$ μm (New Surgical Technologies, Russia), an erbium-doped fibre laser with $\lambda = 1.56$ μm (IRE-Polus, Russia), and a fibre Raman laser with $\lambda = 1.68$ μm (IRE-Polus, Russia). The radiation power was varied from 4 to 7 W with a step of 0.2 W; the irradiation was performed in cw mode. The power level was monitored by a UP12-H power meter (Gentec Electro-Optics).

The temperature field dynamics was recorded using an infrared camera FLIR A655*sc with an FOL25 lens at a frame rate up to 200 Hz. The operating spectral range of the camera is 7.5–14 μm, which overlaps significantly the blackbody emission spectra at temperatures of 25–96°C. The FLIR Research IR Max software was used to process thermograms and determine the maximum temperature obtained on the venous wall outer surface during laser irradiation. It was proved in a separate experiment that coating of cartilaginous tissue by a 100-μm-thick polypropylene film at temperatures of 40–95°C does not cause any significant changes in the infrared imager readings. Indeed, the surface temperature of the thin film contacting the biological tissue is in fact equal to the temperature of upper tissue layers; this result was quite expected. Three experiments on different vein segments were performed for each set of laser radiation parameters (wavelength and power).

After the laser treatment, three samples with masses of 5–8 mg for thermal analysis and two samples for morphological analysis were extracted from the central part (25 mm long) of each vein segment.

Thermal analysis of the samples was performed on a differential scanning calorimeter Phoenix DSC 204 (Netzsch, Germany). The samples were hermetically sealed in standard aluminium pans with a volume of 20 μL. The initial and final temperatures were 20 and 90°C, respectively; the heating rate was 10 K min^{-1}. The thermograms were processed using the NETZSCH Proteus Thermal Analysis software.

To perform morphological analysis, samples were fixed in 10% neutral formalin, and 4-μm-thick paraffin sections were prepared; the latter were stained by hematoxylin and eosin according to the standard technique. The sections were analysed with a universal optical microscope LEICA DM4000 B LED (Leica Microsystems, Switzerland). Micrographs were obtained using a digital video camera LEICA DFC7000 T equipped with the LAS V4.8 software.

Statistical processing. Using the FLIR Research IR Max software, we determined in each frame the maximum temperature obtained on the outer venous wall surface during the laser impact at the instant corresponding to the given frame. This value was averaged (using the OriginPro 2015 software) over 50 frames corresponding to the temperature fields when transmitting the fibre through the central (3.5 cm) part of the processed vein segment. This procedure was performed for three segments exposed to radiation with the same set of parameters to obtain the mean value of maximum temperature and its standard deviation. Three vein segments were processed for each set of laser radiation parameters (wavelength and power).

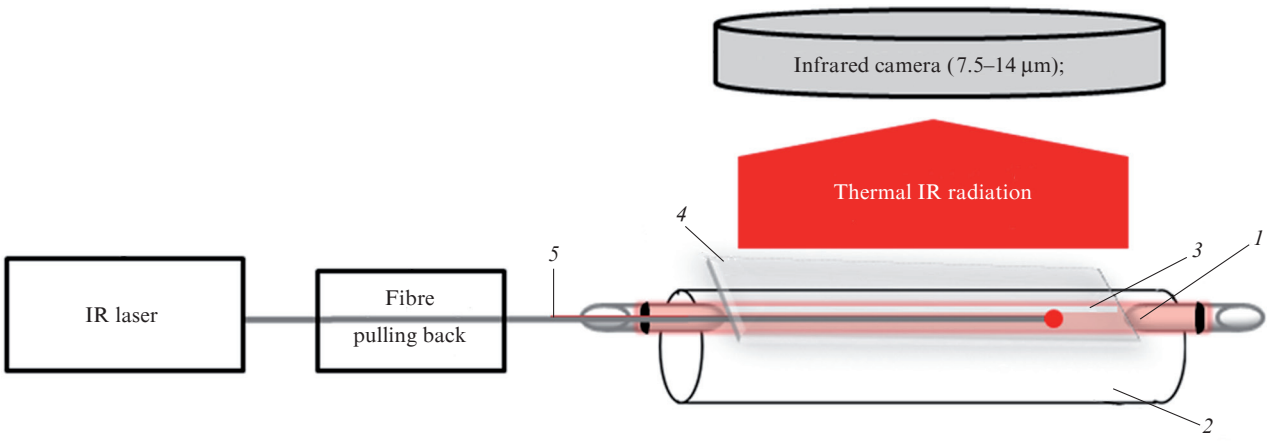

Figure 1. (Colour online) Schematic of the experimental setup: (*1*) vein; (*2*) plastic container; (*3*) slit; (*4*) propylene film; (*5*) optical fibre.

3. Results

The collagen in the intact samples of the venous wall is in the native state, and the thermograms obtained by differential scanning calorimetry (DSC) exhibit a peak at 65°C [Fig. 2, curve (*1*)]. This peak corresponds to denaturation of the structure-forming protein collagen; the area under the curve fragment with peak is proportional to the amount of initial native protein [14]. After the laser impact, with an increase in the power (and, correspondingly, the maximum temperature of the vein surface), the aforementioned area decreases [Fig. 2, curve (*3*)]. At some critical laser power P_c, the collagen denaturation peak disappeared in the DSC thermograms of the samples taken from any irradiated region of vein segment [Fig. 2, curve (*2*)]. This means that the laser effect initiated complete collagen denaturation throughout the entire thickness of the vein wall.

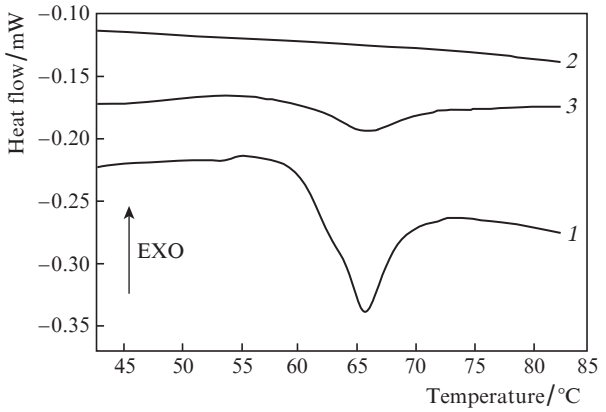

Figure 2. Typical DSC thermograms of varicose vein wall: (*1*) intact sample and (*2*, *3*) samples after laser irradiation with powers equal to P_c (*2*) and below P_c (*3*).

Table 1 contains the P_c values and the corresponding maximum surface temperatures T_c for all laser wavelengths used for tissue heating. The critical powers were different for different wavelengths, whereas the T_c value remained approximately the same: ~91°C. Effective absorption coefficients μ_{eff} were calculated from the known absorption and scattering coefficients of blood for the aforementioned wavelengths [15] within the standard approach [1].

Table 1. Laser radiation parameters for different wavelengths.

λ /μm	T_c /°C	P_c /W	μ_{eff} /cm^{-1}	τ_r /s
1.47	91±2	6.0±0.2	49.4	0.07
1.56	91±1	5.0±0.2	24.9	0.28
1.68	92±1	6.0±0.2	16.4	0.66

Note: τ_r is the thermal relaxation time.

Three layers – intima, media, and adventitia – can be identified in the micrographs of varicose vein wall cuts from unirradiated samples (Fig. 3a). All wall layers contain bundles of collagen fibres, and small vessels (*vasa vasorum*) are traced in the adventitia; they provide nutrition of the venous wall tissue.

Typical micrographs of sections after the laser treatment at critical power are shown in Fig. 3b. Note that no fundamental differences were revealed in the morphological changes in tissue after irradiation at different wavelengths and P_c values. The following characteristic features were observed for all samples:

– pronounced coagulation necrosis of the entire vein wall stratum;

– spasm and endothelium desquamation of *vasa vasorum*; and

– intimal tissue vacuolisation.

When EVLO was performed at powers below critical, the DSC thermograms of the samples retained the collagen denaturation peak; i.e., the degree of denaturation of this protein was less than 100% [Fig. 2, curve (*3*)]. The micrographs demonstrate inhomogeneous necrosis, absence of complete homogenisation, and presence of individual *vasa vasorum* (Fig. 3c); the morphological changes in tissue turned out to be identical for all wavelengths in use.

An important feature of the samples irradiated at wavelengths of 1.47, 1.56, and 1.68 μm with the critical power was

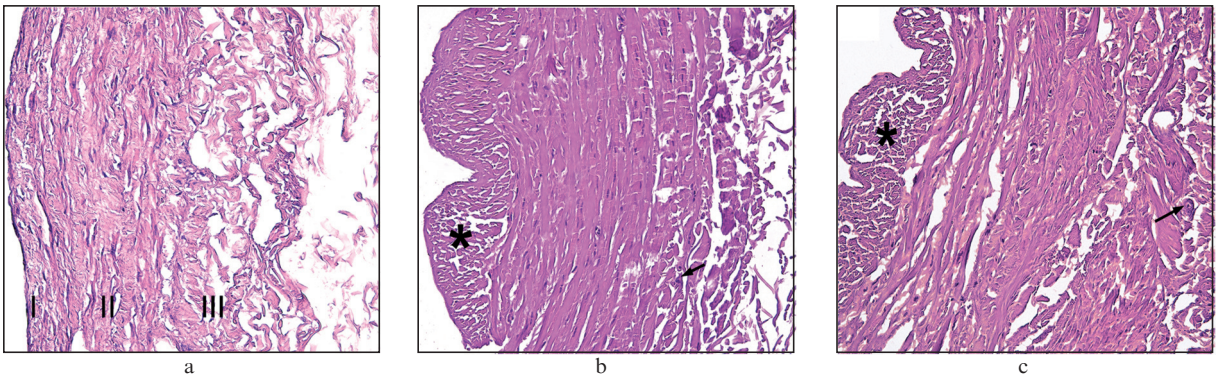

Figure 3. (Colour online) Typical micrographs of (a) intact sample wall of varicose vein and (b, c) varicose vein wall subjected to laser irradiation with powers equal to P_c (b) and below P_c (c): (I) intima, (II) media, and (III) adventitia; asterisk denotes vacuolisation; arrows show *vasa vasorum* regions, stained by hematoxylin and eosin; magnification of 400×.

the absence of perforations and visible carbonised particles, even at the points of direct contact of laser fibre tip with the inner vein wall surface.

4. Discussion

Our main result is the determination of critical powers of laser irradiation with wavelengths 1.47–1.68 μm on the venous wall under EVLO conditions. We found P_c as the power of the laser impact after which thermal analysis shows the absence of denaturation peak in the DSC thermograms of irradiated samples. Complete destruction of the collagen framework throughout the entire venous wall thickness is accompanied by tissue necrosis and *vasa vasorum* spasm. Thus, the irradiation with P_c leads to thermal degradation of the venous wall and tissue shrinkage, i.e., creates all necessary conditions for closing vessel without unnecessary heating of surrounding tissues and provides the ultimate goal: complete obliteration of vein without possibility of its recanalisation. At powers below critical a thermal analysis indicates conservation of a certain fraction of intact collagen fibrous structures. A morphological analysis shows incomplete (focal) necrosis; the absence of homogenisation; and, what is most important, conservation of individual *vasa vasorum* in the vein wall. Thus, if the denaturation is incomplete, other structural elements of tissue are also retained. This poses a threat of subsequent vein obliteration and possibility of inconsistent vessel recanalisation [6]. Hence, the issue about the ultimate effect of the procedure remains unresolved.

Complete collagen denaturation in a venous wall under EVLO conditions, using laser radiation with any wavelength, occurs at a temperature $T_c = 91 \pm 2$ °C. This fact confirms that the destruction of collagen framework during EVLO is due to the thermal effect of laser irradiation [3, 5]. Critical powers differ for laser radiations with different wavelengths. Let us discuss the reason for these differences from the point of view of the efficiency of energy delivery in the form of heat from the fibre tip to a venous wall.

Under laser irradiation from the fibre tip moving in a vein segment, the venous wall is heated by the heat flow in the direction from the carbonised blood coagulum on the tip [4, 5, 7–9]; a critical factor for venous wall heating is the coagulum formation. The coagulation begins with denaturation of plasma proteins, aggregation of erythrocytes, and destruction of cellular membranes (~80 °C) [16]. As a result, a coagulum arises on the fibre tip [16, 17]; its organic components decompose with the formation of carbon in the temperature range of 250–450 °C [18]. This carbonised coagulum absorbs a large fraction of radiation at almost any wavelength and gets hot up to 700–1000 °C [8]. In this case the factors responsible for the dependence of P_c on the wavelength of the laser radiation absorbed by blood are determined to a great extent by the possibility of reaching a high temperature in the volume directly adjacent to the fibre tip. If the irradiation time τ_{irr} is sufficiently short to assume that the absorbed energy is entirely converted into heat, the increase in temperature ΔT in the small impact region will depend on the output radiation power P and effective absorption coefficient μ_{eff} as $\Delta T \approx P\mu_{eff}$ [1]. Since the increase in temperature ΔT necessary for coagulum formation is constant and determined by the properties of the medium rather than the radiation wavelength, $P_c \sim 1/\mu_{eff}$; i.e., the critical power should decrease with an increase in the effective absorption coefficient. However, heat may dissipate into the environment during the irradiation time. The characteristic time of this process (thermal relaxation time) is determined as $\tau_r = 1/(4k\mu_{eff}^2)$ (k is the thermal diffusivity) [1] and decreases with an increase in μ_{eff}. Thus, the μ_{eff} value affects the critical power in two ways. On the one hand, a higher absorption in unit volume increases the temperature in it and, as a consequence, reduces P_c. At the same time, at large μ_{eff} values, the absorbed energy dissipates fairly rapidly due to the heat transfer.

The irradiation time τ_{irr} under the EVLO conditions, which is determined by the fibre velocity, amounts to ~0.5 s [13], a value which comparable with the thermal relaxation time. Hence, both effects (energy absorption and dissipation) make comparable contributions. The data compiled in Table 1 for all wavelengths used indicate that the μ_{eff} value in the wavelength series 1.47–1.56–1.68 μm decreases in a ratio of 11.98 : 1 : 0.66, and the thermal relaxation time τ_r increases from 0.07 to 0.66 s. This means that the effect related to energy absorption becomes weaker, which should lead to an increase in P_c; however, this does not occur, because the energy dissipation rate decreases simultaneously. As a result of the superposition of these effects, the minimum critical power is observed for $\lambda = 1.56$ μm.

5. Conclusions

We determined the critical powers P_c for laser irradiation with wavelengths of 1.47, 1.56, and 1.68 μm at $\mu_{eff} = 49.4$, 24.9, and 16.4 cm^{-1}, respectively, on the venous wall tissue under the conditions close to the EVLO regime with fibre pulled through a blood-filled venous vessel. When achieving P_c, the temperature of the outer venous wall surface reaches 91 ± 2 °C. Under these conditions, the venous wall collagen becomes completely denaturated, tissue necrosis occurs throughout the entire volume, and *vasa vasorum* is destroyed, due to which the target effect of the procedure is provided and impossibility of vessel recanalisation in future is guaranteed. The value $P_c = 5$ W is minimum for the radiation with $\lambda = 1.56$ μm. We explain this result by the fact that the coagulum formation on the fibre tip is critical for venous wall heating. The T_c value is achieved due to the simultaneously occurring processes of energy absorption and dissipation in the form of heat. In turn, their efficiency depends oppositely on the absorption coefficient. The oppositely directed influence of μ_{eff} on T_c can explain the existence of extremum in the dependence of P_c on the laser wavelength.

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